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Kimberly H. Lu  
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Reg. No. 51,973

**Application of:** Bajaj, S. Paul      **Group No.:** 1653

**Serial No.:** 10/662,784      **Atty. Docket No.:** 66153-39722

**Filed:** September 15, 2003

**For:** *REGION OF FACTOR IXa  
PROTEASE DOMAIN  
THAT INTERACTS WITH  
FACTOR VIIa AND  
METHODS THEREFOR*      **Examiner:** Not Yet Assigned

Commissioner of Patents and Trademarks  
P.O. Box 1450  
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HONORABLE SIR:

The present application is a continuation in part of U.S. application no. 09/584,866 (Patent No. 6,624,289 B1). Pursuant to the MPEP § 609.I.A.2, Applicant is not providing copies of the references listed in the enclosed Information Disclosure Statement. According to this section of the MPEP, references that have been considered by the U.S.P.T.O. in the parent application need not be resubmitted.

Respectfully submitted,

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**TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT**  
**(Under 37 CFR 1.97(b) or 1.97(c))**

Docket No.  
66153-39722

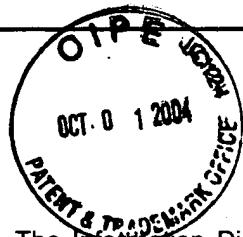
In Re Application Of:

Bajaj, S. Paul

Serial No.	Filing Date	Examiner	Group Art Unit
10/662,784	September 15, 2003	Not Yet Assigned	1653

Title:

**REGION OF FACTOR IXa PROTEASE DOMAIN THAT INTERACTS WITH FACTOR VIIIa AND METHODS THEREFOR**



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**37 CFR 1.97(b)**

1.  The Information Disclosure Statement submitted herewith is being filed within three months of the filing of a national application other than a continued prosecution application under 37 CFR 1.53(d); within three months of the date of entry of the national stage as set forth in 37 CFR 1.491 in an international application; before the mailing of a first Office Action on the merits, or before the mailing of a first Office Action after the filing of a request for continued examination under 37 CFR 1.114.

**37 CFR 1.97(c)**

2.  The Information Disclosure Statement submitted herewith is being filed after the period specified in 37 CFR 1.97(b), provided that the Information Disclosure Statement is filed before the mailing date of a Final Action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an Action that otherwise closes prosecution in the application, and is accompanied by one of:

the statement specified in 37 CFR 1.97(e);

**OR**

the fee set forth in 37 CFR 1.17(p).

Per 37 CFR §1.98(d), copies of the references cited in the accompanying Information Disclosure Statement are not provided herewith because such references were previously cited by or submitted to the Patent and Trademark Office in a parent application to which this application relies upon for an earlier filing date under 35 U.S.C. §120.

**TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT**  
 (Under 37 CFR 1.97(b) or 1.97(c))

Docket No.  
 66153-39722

In Re Application:

Bajaj, S. Paul

Serial No.

10/662 784

Filing Date

September 15, 2003

Examiner

Not Yet Assigned

Group Art Unit

1653



**Payment of Fee**

(Only complete if Applicant elects to pay the fee set forth in 37 CFR 1.17(p))

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				Application Number	10/662,784
				Filing Date	September 15, 2003
				First Named Inventor	Bajaj, S. Paul
				Art Unit	1653
				Examiner Name	Not Yet Assigned
1	of	5	Attorney Docket Number	66153-39722	

U.S. PATENT DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
		US- 5,932,706	08-03-1999	Mertens et al.	
		US-			
		US-			

FOREIGN PATENT DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)			
		WO 93/09804	05-27-1993	Griffin et al.	
		WO 94/25482	11-10-1994	Evans et al.	

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			
		MATHUR et al., Protease and EGF1 domains of factor IXa play distinct roles in binding to factor VIIIa, J. Biol. Chem., 1999, 274(26): 18477-18486			
		YOSHITAKE et al., Nucleotide sequence of the gene for human factor IX (antihemophilic factor B), Biochemistry, 1985, 24: 3736-3750			
		DiSCIPIO et al., Activation of human factor IX (Christmas factor), J. Clin. Invest., 1978, 61: 1528-1538			
		DAVIE et al., The coagulation cascade: initiation, maintenance, and regulation, Biochemistry, 1991, 30: 10363-10370			

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<sup>2</sup> Applicant's unique citation designation number (optional). <sup>3</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>4</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>5</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>6</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>7</sup> Applicant is to place a check mark here if English language Translation is attached.

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				Application Number	10/662,784
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				First Named Inventor	Bajaj, S. Paul
				Group Art Unit	1653
Examiner Name	Not Yet Assigned				
Sheet	2	of	5	Attorney Docket Number	66153-39722

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Examiner Initials	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published			
		BRANDSTETTER et al., X-ray structure of clotting factor IXa: active site and module structure related to Xase activity and hemophilia B., Proc. Natl. Acad. Sci. USA, 1995, 92: 9796-9800			
		BANNER et al., The crystal structure of the complex of blood coagulation factor VIIa with soluble tissue factor, Nature, 1996, 380: 41-46			
		SABHARWAL et al., Interaction of calcium with native and decarboxylated human factor X. Effect of proteolysis in the autolysis loop on catalytic efficiency and factor Va binding, J. Biol. Chem., 1997, 272: 22037-22045			
		RAO et al., The structure of a Ca(2+)-binding epidermal growth factor-like domain: its role in protein-protein interactions, Cell, 1995, 82: 131-141			
		BAJAJ et al., Antibody-probed conformational transitions in the protease domain of human factor IX upon calcium binding and zymogen activation: putative high-affinity Ca(2+)-binding site in the protease domain, Proc. Natl. Acad. Sci. USA, 1992, 89: 152-156			
		FREEDMAN et al., Identification of the phospholipid binding site in the vitamin K-dependent blood coagulation protein factor IX, J. Biol. Chem., 1996, 271: 16227-16236			
		ZHONG et al., First epidermal growth factor-like domain of human blood coagulation factor IX is required for its activation by factor VIIa/tissue factor but not by factor XIa, Proc. Natl. Acad. Sci. USA, 1994, 91: 3574-3578			
		LENTING et al., Ca2+ binding to the first epidermal growth factor-like domain of human blood coagulation factor IX promotes enzyme activity and factor VIII light chain binding, J. Biol. Chem., 1996, 271: 25332-25337			
		AHMED et al., The role of the second growth-factor domain of human factor IXa in binding to platelets and in factor-X activation, Biochem. J., 1995, 310: 427-431			
		ASTERMARK et al., The gamma-carboxyglutamic acid and epidermal growth factor-like modules of factor IXa beta. Effects on the serine protease module and factor X activation, J. Biol. Chem., 1994, 269: 3682-3689			
		O'BRIEN et al., Localization of factor IXa and factor VIIIa interactive sites, J. Biol. Chem., 1995, 270: 27087-27092			

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				First Named Inventor	Bajaj, S. Paul
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		BAJAJ et al., Human factor IX and factor IXa, Methods Enzymol., 1993, 222: 96-128			
		MATHUR et al., Interaction of factor IXa with factor VIIIa. Effects of protease domain Ca2+ binding site, proteolysis in the autolysis loop, phospholipids, and factor X, J. Biol. Chem., 1997, 272: 23418-23426			
		HAMAGUCHI et al., The role of amino-terminal residues of the heavy chain of factor IXa in the binding of its cofactor, factor VIIIa, Blood, 1994, 84: 1837-1842			
		RIPKA et al., Peptidomimetic design, Current Opin. Chem. Biol., 1998, 2(4): 441-452			
		WOOD et al., Expression of active human factor VIII from recombinant DNA clones, Nature, 1984, 312: 330-337			
		VEHAR et al., Structure of human factor VIII, Nature, 1984, 312: 337-342			
		BAJAJ et al., A simplified procedure for purification of human prothrombin, factor IX and factor X, Prep. Biochem., 1981, 11: 397-412			
		ZHONG and BAJAJ, A PCR-based method for site-specific domain replacement that does not require restriction recognition sequences, Biotechniques, 1993, 15: 874-878			
		USHARANI et al., Characterization of three abnormal factor IX variants (Bm Lake Elsinore, Long Beach, and Los Angeles) of hemophilia-evidence for defects affecting the latent catalytic site, J. Clin. Invest., 1985, 75: 76-83			
		LINK and CASTELLINO, The activation of bovine factor X by bovine factor Xa, Arch. Biochem. Biophys., 1982, 215: 215-221			
		VAN DIEIJEN et al., The role of phospholipids and factor VIIIa in the activation of bovine factor X, J. Biol. Chem. 1981, 256: 3433-3442			

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Sheet	4	of	5	Attorney Docket Number	66153-39722

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		FAY and KOSHIBU, The A2 subunit of factor VIIa modulates the active site of factor IXa, J. Biol. Chem., 1998, 273: 19049-19054	
		KRISHNASWAMY, The interaction of human factor VIIa with tissue factor, J. Biol. Chem., 1992, 267: 23696-23706	
		HALFMAN, Concentrations of binding protein and labeled analyte that are appropriate for measuring at any analyte concentration range in radioimmunoassays, Meth. Enzymol., 1981, 74: 481-508	
		BYLUND and TOEWS, Radioligand binding methods: practical guide and tips, Am. J. Physiol., 1993, 265: L421-L42	
		REES et al., The role of beta-hydroxyaspartate and adjacent carboxylate residues in the first EGF domain of human factor XI, EMBO J., 1988, 7: 2053-2061	
		HUGHES et al., Tyrosine 69 of the first epidermal growth factor-like domain human factor IX is essential for clotting activity, J. Biol. Chem., 1993, 268: 17727-17733	
		FRAZIER et al., Mapping of monoclonal antibodies to human factor IX, Blood, 1989, 74: 971-977	
		LUDWIG et al., Hemophilia B caused by five different nondeletion mutations in the protease domain of factor IX, Blood, 1992, 79: 1225-1232	
		GIANNELLI et al., Haemophilia B: database of point mutations and short additions and deletions—eighth edition, Nucleic Acids Res., 1998, 26: 265-268	
		MATHER et al., The 2.8 Å crystal structure of Gla-domainless activated protein C, EMBO J., 1996, 15: 6822-6831	
		BAJAJ et al., Synthesis and expression of tissue factor pathway inhibitor by serum-stimulated fibroblasts, vascular smooth muscle cells and cardiac myocytes, Thrombos. Haemostas., 1999, 82: 1663-1672	

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		CHANG et al., Changing residue 338 in human factor IX from arginine to alanine causes an increase in catalytic activity, J. Biol. Chem., 1998, 273: 12089-12094		
		LIN et al., Expression and characterization of human factor IX and factor IX-factor X chimeras in mouse C127 cells, J. Biol. Chem., 1990, 265: 144-150		
		CHANG et al., Replacing the first epidermal growth factor-like domain of factor IX with that of factor VII enhances activity in vitro and in canine hemophilia B, J. Clin. Invest., 1997, 100: 886-892		
		SPITZER et al., Factor IX Hollywood: substitution of Pro55 by Ala in the first epidermal growth factor-like domain, Blood, 1990, 76: 1530-1537		
		McCCORD et al., Characterization of the functional defect n factor IX Alabama, J. Biol. Chem., 1990, 265: 10250-10254		
		CHRISTOPHE et al., Blood coagulation factor IX residues Glu78 and Arg94 provide a link between both epidermal growth factor-like domains that is crucial in the interaction with factor VIII light chain, J. Biol. Chem., 1998, 273: 222-227		
		LARSON et al., Structural integrity of the gamma-carboxyglutamic acid domain of human blood coagulation factor IXa is required for its binding to cofactor VIIa, J. Biol. Chem., 1996, 271: 3869-3876		
		SABHARWAL et al., High affinity Ca(2+)-binding site in the serine protease doma of human factor VIIa and its role in tissue factor binding and development of catalytic activity, J. Biol. Chem., 1995, 270: 15523-15530		
		BAJAJ et al., A monoclonal antibody to factor IX that inhibits the factor VII:Ca potentiation of factor X activation, J. Biol. Chem., 1985, 260: 11574-11580		

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